

APPENDIX I
CURRENTLY PENDING CLAIMS

23. (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, with the proviso that the protein stabilizing agent is not congo red, DMSO or glycerol.

24. (New) The method according to claim 23, wherein the defective target protein is the gene product of a naturally occurring mutant nucleic acid.

25. (New) The method according to claim 23, wherein the defective target protein is the gene product of a heterologous nucleic acid.

26. (New) The method according to claim 23, wherein the defective target protein is selected from the group consisting of the cystic fibrosis transmembrane conductance regulator (CFTR) protein, emphysema and chronic liver disease α -1 anti-trypsin inhibitor, LDL receptor (familial hypercholesterolemia), β -hexylaminidase (Tay-sachs), fibrillin (Marfan syndrome) superoxide dismutase (amyotrophic lateral sclerosis), collagen (scurvy), α -ketoacid dehydrogenase complex (maple syrup urine disease), p53 (cancer), type I procollagen pro- α (osteogenesis imperfecta), β -amyloid (Alzheimer's disease), crystallins (cataracts), rhodopsin (retinitis pigmentosa), and insulin receptor (leprechaunism).

27. (New) The method according to claim 23, wherein the protein stabilizing agent is selected from the group consisting of deuterated water, polyols and sugars, including erythritol, inositol, trehalose isofluoroside, polyethylene glycol,

amino acids and derivatives thereof, including glycine, alanine, proline, taurine, betaine, octopine, glutamate, sarcosine, gamma-aminobutyric acid, and trimethylamine N-oxide (TMAO).

28. (New) The method according to claim 23, wherein the phenotypic defect is caused by a condition selected from the group consisting of improper folding, improper co- and post-translational modification, improper subcellular targeting, inability to bind biological ligands, aggregation, proteolytic degradation, temperature sensitive folding, and any combination thereof.

29. (New) The method according to claim 28, wherein the condition that causes the phenotypic defect occurs in a part of the protein that is selected from the group consisting of pre-sequence, pro-sequence, and mature protein sequence.

30. (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, and wherein the conformational defect is a temperature sensitive folding defect, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, with the proviso that the protein stabilizing agent is not congo red, DMSO or glycerol.

31. (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, and wherein the defective target protein is an enzyme, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second

cell is not contacted with the protein stabilizing agent, with the proviso that the protein stabilizing agent is not congo red, DMSO or glycerol.

32. (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, and wherein the conformational defect causes improper protein targeting, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, with the proviso that the protein stabilizing agent is not congo red, DMSO or glycerol.

33. (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, and wherein the protein stabilizing agent is trimethylamine N-oxide.

34. (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, and

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wherein the protein stabilizing agent is an amino acid or derivative thereof, including glycine, alanine, proline, taurine, betaine, octopine, glutamate, sarcosine, gamma-aminobutyric acid, and trimethylamine N-oxide (TMAO).

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